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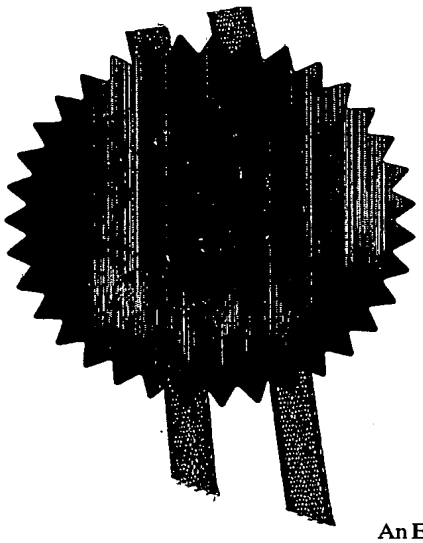

Signed Stephen Hardley

Dated 11 August 2004

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1. Your reference PZ0362 GB

2. Patent application number *(The Patent Office will fill in this part)* 31 JUL 2003 0317920.7

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

AMERSHAM PLC
Amersham Place
Little Chalfont
Buckinghamshire HP7 9NA

Patents ADP number *(if you know it)*

If the applicant is a corporate body, give the country/state of its incorporation United Kingdom

8189375004

4. Title of the invention

SOLID-PHASE SYNTHESIS

5. Name of your agent *(if you have one)*

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

HAMMETT, Audrey, Grace, Campbell ; ROLLINS, Anthony, John; HAMMER, Catriona, MacLeod and BRYAN, Ian, Bennett
Amersham plc
Amersham Place
Little Chalfont
Buckinghamshire HP7 9NA

Patents ADP number *(if you know it)*

8189375004

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Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*

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a) any applicant named in part 3 is not an inventor, or
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11. I/We request the grant of a patent on the basis of this application.

Signature: Audrey Hammett
HAMMETT, Audrey, Grace, Campbell

Date: 30 July 2003

12. Name and daytime telephone number of person to contact in the United Kingdom: HALLS, Jennie 01494 542032

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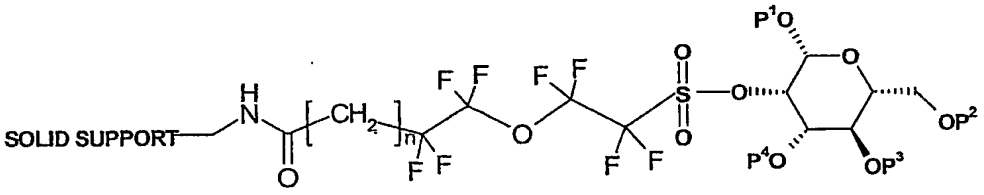
SOLID-PHASE SYNTHESIS

The present invention relates to novel intermediates for solid-phase production of 2-[^{18}F]- fluoro-2-deoxy-D-glucose (^{18}F-FDG), a Positron Emission Tomography (PET) radiotracer, and radiofluorination processes using these intermediates. The invention also comprises radiopharmaceutical kits using these novel processes and intermediates.

The favoured radioisotope for PET, ^{18}F, has a relatively short half-life of 110 minutes. ^{18}F-labelled tracers for PET therefore have to be synthesised and purified as rapidly as possible, and ideally within one hour of clinical use. Standard synthetic methods for introducing fluorine-18 are relatively slow and require post-reaction purification (for example, by HPLC) which means that it is difficult to obtain the ^{18}F-labelled tracer for clinical use in good radiochemical yield. There is also a need for automation to protect the operator from radiation exposure. Many radiofluorinations are complicated procedures and it is necessary to simplify them to facilitate automation.

WO 03/002157 describes solid-phase processes for producing ^{18}F-labelled tracers quickly and with high specific activity yet avoiding time-consuming purification steps, such that the resultant ^{18}F-labelled tracer is suitable for use in PET. The solid-phase methods also lend themselves to automation with advantages of ease of production and greater throughput. We have now found a particular class of intermediate for production of ^{18}F-FDG falling within the scope of WO 03/002157, but which have advantages including that they can be synthesised in good yields and which give surprisingly good yields in the radiofluorination reaction.

Thus, according to a first aspect of the invention, there is provided a compound of formula (I):



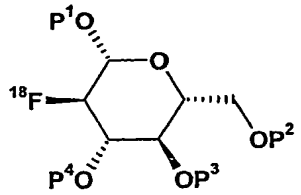
(I)

wherein P^1, P^2, P^3, and P^4 are each independently hydrogen or a protecting group; and n is an integer of from 2 to 20.

In the compounds of formula (I), n is suitably 4 to 12, preferably 6 to 10, and is most preferably 10.

In the compounds of formula (I), suitable protecting groups, P^1, P^2, P^3, and P^4 may be found, for example, in Protecting Groups in Organic Synthesis, Theordora W. Greene and Peter G. M. Wuts, published by John Wiley & Sons Inc.. P^1 is preferably C_{1-4} alkyl, such as methyl. P^4 is preferably C_{1-4} alkoxymethyl, such as ethoxymethyl. P^2 and P^3, together with the oxygens to which they are attached, suitably form a 1,3-dioxolane, such as a 2-phenyl 1,3-dioxolane (a benzylidene protecting group).

The present invention provides, in a further aspect, a process for the production of 2-^{18}F-fluoro-2-deoxy-D-glucose (^{18}F-FDG) which comprises treatment of a solid support-bound precursor of formula (I) as defined above,
with $^{18}F^-$ to produce the labelled tracer of formula (II)



(II)

wherein P^1, P^2, P^3, and P^4 are each independently hydrogen or a protecting group;

optionally followed by

(i) removal of excess $^{18}F^-$, for example by ion-exchange chromatography; and/or

(ii) removal of the protecting groups; and/or

(iii) removal of organic solvent; and/or

(iv) formulation of the resultant compound of formula (II) as an aqueous solution.

As the ^{18}F-labelled tracer of formula (II) is removed from the solid-phase into solution, all unreacted precursor remains bound to the resin and can be separated by simple filtration, thus obviating the need for complicated purification, for example by HPLC. The ^{18}F-labelled tracer of formula (II) may be cleaned up by removal of excess F^-, for example by ion-exchange chromatography and/or by removal of any organic solvent. The resultant ^{18}F-FDG may then be further made-up into an aqueous formulation for clinical use.

In the compounds of formula (I) the "SOLID SUPPORT" may be any suitable solid-phase support which is insoluble in any solvents to be used in the process but to which the linker can be covalently bound. Examples of suitable SOLID SUPPORT include polymers such as polystyrene (which may be block grafted, for example with polyethylene glycol), polyacrylamide, or polypropylene or glass or silicon coated with such a polymer. The solid support may be in the form of small discrete particles such as beads or pins, or as a coating on the inner surface of a cartridge or on a microfabricated vessel.

Treatment of the compound of formula (I) with $^{18}F^-$ may be effected by treatment with any suitable source of $^{18}F^-$, such as $Na^{18}F$, $K^{18}F$, $Cs^{18}F$, tetraalkylammonium ^{18}F fluoride, or tetraalkylphosphonium ^{18}F fluoride. To increase the reactivity of the fluoride, a phase transfer catalyst such as 4,7,13,16,21,24 hexaoxa-1,10-diazabicyclo[8,8,8] hexacosane may be added and the reaction performed in a non protic solvent. These conditions give reactive fluoride ions. The treatment with $^{18}F^-$ is suitably effected in the presence of a suitable organic solvent such as acetonitrile, dimethylformamide, dimethylsulphoxide, tetrahydrofuran, dioxan, 1,2 dimethoxyethane, sulpholane, N-methylpyrolidinineone, at a non-extreme

temperature, for example, 15°C to 180°C, preferably at elevated temperature. On completion of the reaction, the ^{18}F-labelled tracer of formula (II) dissolved in the solvent is conveniently separated from the solid-phase by filtration.

Any excess $^{18}F^-$ may be removed from the solution of ^{18}F-FDG by any suitable means, for example by ion-exchange chromatography or solid phase absorbents. Suitable ion-exchange resins include BIO-RAD AG 1-X8 or Waters QMA and suitable solid phase absorbents include alumina. The excess $^{18}F^-$ may be removed using such solid phases at room temperature in aprotic solvents.

Removal of any protecting groups from the compound of formula (II) may be effected by standard methods. Suitable protection and deprotection methodologies may be found, for example, in Protecting Groups in Organic Synthesis, Theodora W. Greene and Peter G. M. Wuts (see above). In a preferred embodiment of the invention, the sugar hydroxyl groups are protected as esters, suitably C_{1-6} alkanoic esters, preferably as acetate esters, or as ethers, preferably C_{1-6}alkoxy methyl ethers, or acetals. Ester, acetal, or ether protecting groups may be conveniently removed by hydrolysis, for example in the presence of acid or base. Such deprotection may be effected on using solid supported acid or base catalysts that render the need for post deprotection neutralisation unnecessary

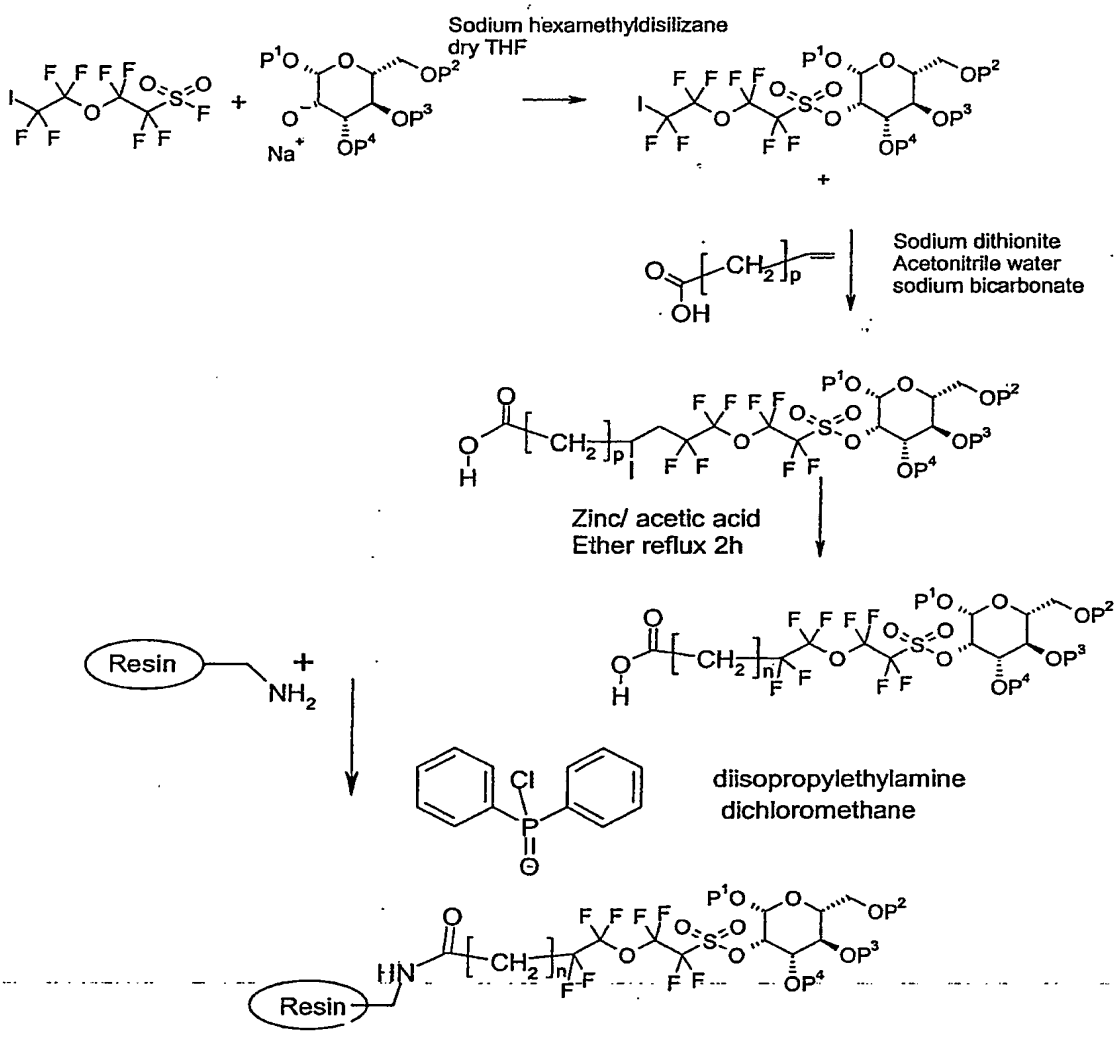
Any organic solvent may be removed by any standard method such as by evaporation at elevated temperature *in vacuo* or by passing a stream of inert gas such as nitrogen or argon over the solution.

Before use of the ^{18}F-FDG, it may be appropriate to formulate it, for example as an aqueous solution by dissolving the ^{18}F-labelled tracer in sterile isotonic saline which may contain up to 10% of a suitable organic solvent such as ethanol, or a suitable buffered solution such as phosphate buffer. Other additives may be added such as ascorbic acid to reduce radiolysis.

Compounds of formula (I) may be prepared by the method shown in Scheme 1 in

which n, P^1, P^2, P^3 and P^4 are as defined for the compound of formula (I) and p is n-2.

Scheme 1



As described above, the advantages of such solid-phase processes for preparation of ^{18}F-labelled tracers include the relative speed of the process, simplified purification methods and ease of automation- all of which mean that the processes are suitable for preparation of ^{18}F-labelled tracers for use in PET. Accordingly, the present invention provides the use of a process for the

manufacture of ^{18}F-FDG for use in PET.

Conveniently, the solid support bound precursor of formula (I) could be provided as part of a kit to a radiopharmacy. The kit may contain a cartridge which can be plugged into a suitably adapted automated synthesiser. The cartridge may contain, apart from the solid support-bound precursor, a column to remove unwanted fluoride ion, and an appropriate vessel connected so as to allow the reaction mixture to be evaporated and allow the product to be formulated as required. The reagents and solvents and other consumables required for the synthesis may also be included together with a compact disc carrying the software which allows the synthesiser to be operated in a way so as to meet the customers requirements for radioactive concentration, volumes, time of delivery etc.

Conveniently, all components of the kit are disposable to minimise the possibilities of contamination between runs and may be sterile and quality assured.

The invention further provides a radiopharmaceutical kit for the preparation of ^{18}F-FDG for use in PET, which comprises:

(i) a vessel containing a compound of formula (I) ; and

(ii) means for eluting the vessel with a source of $^{18}F^-$;

(iii) an ion-exchange cartridge for removal of excess $^{18}F^-$; and optionally

(iv) a cartridge for solid-phase deprotection of the resultant product of formula (II) .

The invention further provides a cartridge for a radiopharmaceutical kit for the preparation of an ^{18}F-FDG for use in PET which comprises:

(i) a vessel containing a compound of formula (I); and

(ii) means for eluting the vessel with a source of $^{18}F^-$.

In a further aspect of the invention, there is provided a method for obtaining a diagnostic PET image which comprises the step of using a radiopharmaceutical kit or a cartridge for a radiopharmaceutical kit as described above.

The invention will now be illustrated by way of the following Examples.

Throughout the Examples, abbreviations used are as follows:

DMF: N,N-dimethylformamide

w/v : weight/volume

h : hour(s)

TLC : thin layer chromatography

THF : tetrahydrofuran

eq. : equivalents

DCM: dichloromethane

EtOAc : ethyl acetate

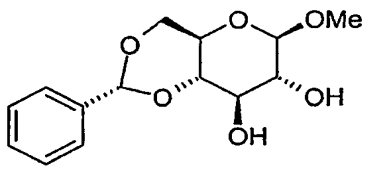
min(s): minute (s)

Examples

Intermediate 1: Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (5-Iodooctafluoro-3-oxapentanesulphonate) -β-D-mannopyranoside

Intermediate 1(i)

Synthesis of Methyl 4,6-O- benzylidene-β-D-glucopyranoside



All materials unless specifically referred to were supplied by the Aldrich chemical company.

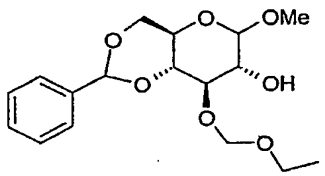
Using a modification of the procedure as described: Tetrahedron, 1992, 48(47), 10249-10264. Methyl β-D-glucopyranoside (Biosynth International M-3592; 10.2g, 50mmol), benzaldehyde dimethylacetal (30ml, 200mmol) and 10-camphorsulfonic acid (116mg, 0.5mmol) in anhydrous acetonitrile (150ml) was stirred at room temperature for 4h. The reaction was checked by TLC to confirm complete conversion to the product (run in hexane: ethyl acetate, 1:2, visualised

with ceric ammonium molybdate spray and heating. The reaction was then treated with triethylamine (1ml) to neutralise the acid. The solution was filtered and the solid was washed with acetonitrile (20ml). The mother solution was concentrated to about 60ml, and it was again filtrated, and the filtrate washed with acetonitrile (10ml). The combined solid was dried in vacuum, to give 12.9g (91%) of methyl 4,6-O-benzylidene-β-D-glucopyranoside.

^{1}H NMR $(CD_3)_2SO$ (300 MHz) TMS ref. δ 3.09(1H, q); 3.42(7H, m); 3.69(1H, t,); 4.18(1H, t,t); 5.35(2H, d,d); 5.57(1H, s,); 7.37 (3H, m);7.45 (2H, m).

^{13}C NMR $(CD_3)_2SO$ (300 MHz) TMS ref. δ: 56.4, 65.78, 67.97, 72.81, 74.27, 80.63, 100.67, 104.53, 126.35, 128.03, 128.85, 137.80

Intermediate 1 (ii)
Methyl 4,6-O- benzylidene-3-ethoxymethy-*β*-D-glucopyranoside



In a 5L round bottomed flask equipped with an overhead stirrer and held under an atmosphere of nitrogen was placed dry methyl 4,6-O-benzylidene-*β*-D-glucopyranoside (50g, 175mmole) and dry tetrahydrofuran (3.5L) (Aldrich chromatography grade) and the mixture stirred at room temperature until the sugar had dissolved. Sodium hydride, (16.5g of a 60% suspension in oil, 0.41mole, 2.36eq) was then added with stirring in small portions whilst there was a vigorous evolution of hydrogen over a period of 15 min. When the sodium hydride is added to the methyl 4,6-O-benzylidene-*β*-D-glucopyranoside, effervescence is vigorous. It should therefore be added in smaller portions to ensure that the effervescence does not exceed the capacity of the flask. Only a minor exotherm was observed (~3°C). The reaction became quite viscous at this point.

Ethoxy methyl chloride (20g, 19.3ml, 0.2127mole, 1.21eq) was dissolved in dry THF (100ml) and added via a dropping funnel to the reaction mixture over a period

of 15 min and stirring was continued for 20h at room temperature. The reaction was then monitored by TLC ethyl acetate; visualised with ceric ammonium molybdate spray, appendix (a). The TLC gave 4 spots.

2,3-Dialkylated sugar	RF 0.78
2-alkylated product	RF 0.52
3-alkylated product	RF 0.26
Starting material	RF 0.04

The amount of starting material had been reduced almost to nothing after 20h and the reaction was worked up. The reaction was cautiously quenched by the dropwise addition of water (10ml) to destroy any excess sodium hydride and the resulting solution concentrated in vacuum (to 250ml) partitioned between aqueous saturated sodium hydrogen carbonate (500ml) and ethyl acetate (1L). The upper ethyl acetate layer was separated and dried over sodium sulphate. The aqueous layer was extracted with a further 2 x 500ml of ethyl acetate and the combined ethyl acetate solutions concentrated in vacuum to give a yellow oil (95g).

The product was divided into two and chromatographed in two portions on flash silica (BDH Silica gel for flash chromatography Product 153325 d10- 33um, d90- 70um) (silica gel dimensions 75mm x 300mm, column 75mm diameter 400mm) in a gradient of 40-60 petroleum ether: ethyl acetate. The crude product was dissolved in 2:1 40-60 petroleum ether: ethyl acetate in order to load it onto the flash column. If the reaction is nearly complete all the crude material goes into solution, as only the starting methyl 4,6-O-benzylidene-β-D-glucopyranoside is relatively insoluble in this solvent. The column was eluted sequentially with 2.5L; 2:1 40-60 petroleum ether: ethyl acetate; 2L of 1.5:1 40-60 petroleum ether: ethyl acetate and 2.5L 1:1 40-60 petroleum ether: ethyl acetate. 40 ml Fractions were collected, monitored by TLC 1:1 40-60 petroleum ether: ethyl acetate) and visualised with ceric ammonium molybdate spray, appendix (a). The TLC indicated 4 main products.

The four products were concentrated in vacuum to give:

Fastest running compound: Fractions 24-33. Mineral oil

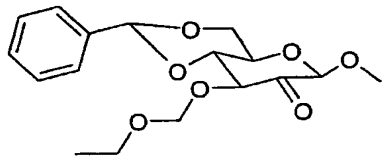
Product 3a: Fractions 40-62. Methyl 4,6-O- benzylidine-2, 3- diethoxymethyl -β-D-glucopyranoside Mwt = 398 Wt 7.689g 0.0193 moles yield 11.0 %

Product 3b: Fractions 73-91. Methyl 4,6-O- benzylidine-2-ethoxymethyl-β-D-glucopyranoside Mwt = 340 Wt 8.73g 0.0256 moles yield 14.6 %
Product 3: Fractions 95-150. Methyl 4,6-O-benzylidine-3-ethoxymethyl-β-D-glucopyranoside Mwt = 340 Wt 32.603g 0.0958moles yield 54.8%

^{1}H NMR $CDCl_3$ (300 MHz) δ 1.25(3H, s), 3.34(1H,t), 3.43 (1H, m), 3.58(5H, m), 3.75(4H, M), 3.92(1H, m), 4.33(2H, d, d), 4.73(1H,d), 4.80(1H, q), 5.53(1H, q), 7.35(3H, m), 7.48(2H, m).

Representing 80% recovery of product.

Intermediate 1 (iii)
Methyl 4,6-O- benzylidene-3-O-ethoxymethyl-2-keto-β-D-glucopyranoside



Methyl 4,6-O-benzylidene-3-ethoxymethyl-β-D-glucopyranoside (prepared as described in Intermediate 1(ii) (14g, 41.2mmoles) was treated with methylsulfoxide (168ml) and acetic anhydride (84.5ml) at room temperature for 24 h. Thin layer chromatography (40-60 hexanes) / Ethyl acetate 1:1 or 100% diethylether) developed with cerium ammonium molybdate and heating (see procedure above) indicated complete conversion to the ketone. The solution was then diluted with ethyl acetate (1l) and washed with thorough shaking in a separating funnel with saturated aqueous potassium carbonate solution (600ml) to hydrolyze the excess acetic anhydride. Caution: Excess potassium carbonate solution must be used as unreacted acetic anhydride can hydrolyze in the water to give acetic acid, which deprotects the sugar. In addition, with insufficient base large amounts of carbon dioxide are liberated causing frothing. The ethyl acetate layer was separated and washed with water (3x500ml) which was sequentially back extracted with ethyl acetate (3x500ml). The ethyl acetate fractions was dried over sodium sulphate and concentrated in vacuum to give a semi crystalline solid, crude methyl 4,6-O-benzylidine-3-ethoxymethyl-2 keto-β-D-glucopyranoside. (~ 20g >100 %

containing ethyl acetate) A sample was crystallised from diethyl ether/petrol ether. From the NMR the compound is mixture of the ketone and water in the solvent, in equilibrium with the diol.

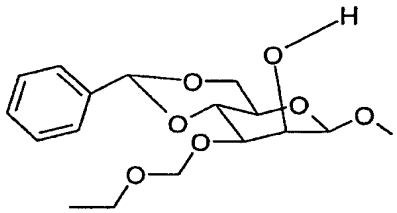
^{1}H NMR $CDCl_3$ (300 MHz) δ; 1.09 and 1.16 (3H, t,); 1.65(1H, s); 2.61(1H, s); 3.45(1H, m,); 4.5 (1H, S,); 4.8 (1H, d); 4.87 (1H, d); 4.95(1H, d,); 5.38 (1H, s,); 5.54 (1H, s,); 7.4 (3H, m,); 7.49(2H, m,);

^{13}C NMR $CDCl_3$ (75 MHz) δ; 14.79, 40.97, 57.19, 57.84, 63.77, 64.37, 64.59, 66.57, 68.55, 78.54, 81.84, 82.94, 92.55, 92.89, 94.9, 101.25, 101.62, 102.93, 126.19, 128.25, 129.11, 136.76, 1327.17.

The crude material contains methyl-2-acetoxy-4, 6-O- benzylidine-3-ethoxymethyl-β-D-glucopyranoside from acetylation of the starting material rather than oxidation. This crude material was used directly in the next step.

Intermediate 1.(iv)

Preparation of Methyl 4,6-O- benzylidene -3-ethoxymethyl -β-D-mannopyranoside



Methyl 4,6-O- benzylidene -3-ethoxymethyl-2 keto-β-D-glucopyranoside (~20g of crude material from the previous step, 0.0412 Mole assuming 100% yield) in methanol (200ml) was treated with sodium borohydride (1.686g, 0.444mmole) at –20°C with continuous stirring and allowed to warm to room temperature over 48h. The reaction was then monitored by TLC (100% diethyl ether) visualised with ceric ammonium molybdate and heating, appendix (a). The ketone has almost the same Rf as the alcohol as it exists as a diol. The reaction was then concentrated in vacuum to a gum and the product partitioned between ethyl acetate (250ml) and dilute aqueous potassium carbonate solution (50 ml). The ethyl acetate layer was

separated and dried over sodium sulfate. The aqueous layer was reextracted with ethyl acetate (2x100ml), dried over the sodium sulphate and the combined ethyl acetate extracts evaporated to give an off white solid. This material was chromatographed on flash silica (BDH Silica gel for flash chromatography Product 153325 d10- 33um, d90- 70um) (silica gel dimensions 75mm x 200mm, column 75mm diameter 400mm) in a gradient of 40-60 petroleum ether: ethyl acetate. The column was eluted sequentially with 2.L; 1:1 40-60 petroleum ether: ethyl acetate; 2L of 1:1.5 40-60 petroleum ether:ethyl acetate and 2.5L ethyl acetate. 40 ml Fractions were collected, monitored by TLC (1:1 40-60 petroleum ether: ethyl acetate) and visualised with ceric ammonium molybdate spray () The TLC indicated 3 main products.

The three products were concentrated in vacuum to give:

Product 1: Fractions 10-30. Methyl 2-acetoxy-4, 6-O- benzylidene-3-ethoxymethyl -β-D-glucopyranoside (1.54g 0.0040mole), 9.8%

Product 2: Fractions 35-48. Methyl 4,6-O- benzylidene-3- ethoxymethyl -β-D-glucopyranoside (2.743g, 0.00806mole), 19.58% Very crude did not crystallise. Probably only 50% compound.

Product 3: Fractions 50-73. Methyl 4,6-O- benzylidene-3-ethoxymethyl -β-D-mannopyranoside (10.62g, 0.0312 mole), 76% over two steps. Crystallisation from ether gave 7.84g of very pure material and 2.78g of solid on evaporation of the mother liquors, which was suitable for use in the next step.

Together representing 105% recovery of product probably reflecting contamination of fraction 2 with dimethylsulphoxide.

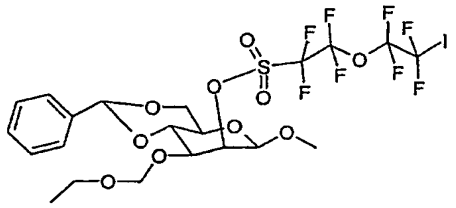
^{1}H NMR $CDCl_3$ (300 MHz) δ: 1.19 (3H, t,) 1.60(1H, s), 2.54(1H, s); 3.39(1H, m,); 3,59(3H, s,); 3.64(2H, m,) 3.77 (2H, m,); 4.09 (1H, t), 4.37(1H, d, d); 4.51 (1H,s,); 4.78 (1H, d,) 4.85, 1H, d,); 5.54(1H, s,); 7.36 (3H, m,) 7.47 (2H, m).

^{13}C NMR $CDCl_3$ (75 MHz) δ ; 14.8, 57.10, 63.41, 66.81, 68.40, 70.07, 74.57, 77.42, 94.51, 101.51, 126.29, 128.54, 128.78, 137.21.

Intermediate 1 (v)

Methyl-4,6-O-benzylidine-3-ethoxymethyl-2-(5-Iodooctafluoro-3-

oxapentanesulphonate) -β-D-mannopyranoside



Methyl 4,6-O-benzylidine-3-ethoxymethyl-β-D-manopyranoside (Intermediate 1(iv)) (1g, 2.93mMole) was dissolved in dry THF (30ml) under dry nitrogen and treated with 1 molar sodium hexamethyldisilizane in THF (4.43ml, 4.43 mmole, 1.5 eq) and stirred for 5 minutes, and then treated with 5-iodooctafluoro-3-oxapentafluorosulphonyl fluoride (Appollo, 1.89g, 4.43mmole). The reaction was stirred at room temperature for 1h. The reaction was monitored by TLC on silica developed in ethyl acetate and visualised by spraying with cerium ammonium molybdate and heating.

The reaction was concentrated in vacuum to low volume, (to remove the excess 5-Iodooctafluoro-3-oxapentafluoro sulphonyl fluoride and the tetrahydrofuran) diluted with ethyl acetate (30ml) and washed with saturated aqueous sodium hydrogen carbonate solution. The organic phase was separated and dried over sodium sulphate and concentrated in vacuum to a gum. The aqueous phase was reextracted with ethyl acetate (2x30ml), the extracts dried over sodium sulphate and the combined ethyl acetate extracts concentrated in vacuum to give Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (5-Iodooctafluoro-3-oxapentanesulphonate) -β-D-mannopyranoside(2.712g).

^{1}H NMR $CDCl_3$ (300 MHz) TMS ref. δ 7.50-7.30 (5H, m, Ph), 5.57 (1H, s, $PhCHO_2$), 5.13 (1H, d, J = 2.9 Hz, H^2), 4.81 (2H, AB, J = 7.4, 21.3 Hz, OCH_2O), 4.57 (1H, s, H^1), 4.34 (1H, dd, J = 5.1, 10.3 Hz, H^6), 4.12 (1H, dd, J = 2.9, 9.6 Hz, H^3), 3.94-3.82 (2H, m, H^4, $H^{6'}$), 3.74-3.55 (2H, m, CH_2), 3.56 (3H, s, CH_3O), 3.44 (1H, ddd, J = 4.4, 9.5, 10.3 Hz, H^5), 1.13 (3H, t, J = 6.6 Hz, CH_3);

^{13}C NMR $CDCl_3$(75 MHz,) TMS ref. δ: 137.13, 129.28, 128.37, 126.19, 101.92 ($PhCHO_2$), 99.16 (C^1), 94.07 (OCH_2O), 83.61 (C^2), 77.32 (C^4), 71.04 (C^3), 68.44 (C^6), 67.58 (C^5), 63.96 (CH_2O), 57.50 (CH_3O), 15.01 (CH_3);

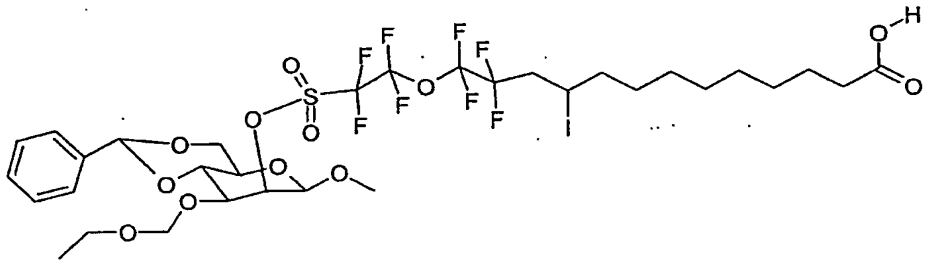
^{19}F NMR $CDCl_3$ (282 MHz) ref. C_6F_6 δ: 96.98, 79.97, 76.42, 48.24.

ν_{max} (film)/cm^{-1} 2973w, 2941w, 1738m, 1413m, 1380m, 1337m, 1295m, 1209s, 1148s, 1094s, 1026s, 917m;

Example 1 : Preparation of Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13 ,15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside amino polystyrene resin amide

Example 1 (i)

Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13 ,15,15,16,16-Octafluoro-10-iodo-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside



Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (5-Iodooctafluoro-3-oxapentane sulphonate -β-D-mannopyranoside (crude Intermediate 1) (2.7g 2.96mmole theoretical) was dissolved in acetonitrile (40ml) water (20ml) cooled to 0°C on an ice bath, stirred and treated with sodium hydrogen carbonate (298mg, 3.55mmole 1.2eq) sodium dithionite (617mg, 3.55 mmole, 1.2 eq) and undecylenic acid (Aldrich, 544mg, 2.96 mmole, 1.0eq). The stirred reaction was allowed to warm to room temperature over 1h. The reaction was monitored by TLC on silica developed in ethyl acetate and visualised by spraying with cerium ammonium molybdate and heating.

The reaction was concentrated at room temperature in high vacuum to 20ml to remove the acetonitrile, and extracted with ethyl acetate (30ml). (The separation of the two layers is rather slow). The ethyl acetate layer was separated and

washed with water (30ml). The aqueous extracts were sequentially reextracted with ethyl acetate (3x30ml) and the combined ethyl acetate extracts were dried over sodium sulphate and concentrated in high vacuum at room temperature to a gum to give Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13 ,15,15,16,16-octafluoro-10-iodo-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside (3.1g). The crude material was used directly in the next step without further purification. The material was stored at –25°C overnight to ensure that it did not decompose. A sample of the compound was purified by chromatography on silica in a gradient of ethyl acetate in petrol to give a pure sample.

^{1}H NMR $CDCl_3$ (300 MHz) TMS ref. δ: 7.50-7.31 (5H, m, Ph), 5.58 (1H, s, $PhCHO_2$), 5.15 (1H, d, J = 2.9 Hz, H^2), 4.80 (2H, AB, J = 7.4 Hz, OCH_2O), 4.61 (1H, s, H^1), 4.40-4.25 (1H, m, CHI, H^6), 4.17 (1H, dd, J = 2.9, 10.3 Hz, H^3), 3.95-3.85 (2H, m, H^4, H^6), 3.75-3.60 (2H, m, CH_2), 3.58 (3H, s, CH_3O), 3.51-3.42 (1H, m, H^5), 3.00-2.65 (2H, m, CH_2), 2.35 (2H, t, J = 7.4 Hz, CH_2), 1.90-1.30 (14H, m, CH_2), 1.15 (3H, t, J = 6.6 Hz, CH_3);

^{13}C NMR $CDCl_3$ (75 MHz) δ: 179.52 (CO), 137.31, 129.51, 128.41, 126.35 (Ph), 102.09 ($PhCHO_2$), 99.37 (C^1), 94.15 (OCH_2O), 83.73 (C^2), 77.48 (C^4), 71.28 (C^3), 68.60 (C^6), 67.79 (C^5), 64.14 (CH_2O), 57.62 (CH_3O), 41.54, 40.58, 34.19, 29.74, 29.41, 29.38, 29.26, 28.71, 24.93 (CH_2), 21.36 (CHI), 15.12 (CH_3);

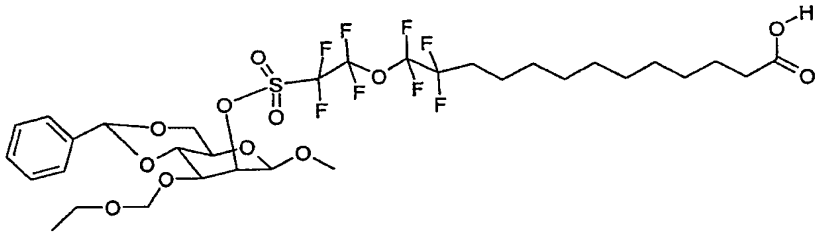
^{19}F NMR $CDCl_3$ (282 MHz), ref. C_6F_6 δ: 79.78, 74.37, 47.92, and 43.70.

m/z (ES^-) 929.3 $[M]^-$.

$\bar{\nu}_{max}$ (film)/cm^{-1} 2972w, 2931w, 2858w, 1709m, 1410m, 1192s, 1147s, 1093s, 1025s, 993s, 919s;

Example 1(ii)

Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13 ,15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside



Methyl-4, 6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13, 15,15,16,16-Octafluoro-10-iodo-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside (prepared as described in Example 1(i))(2.96mmol, 2,75g) was dissolved in dry diethyl ether (40ml) and dry acetic acid (20ml) and treated with zinc powder (1150mg, 17.8mmole, 6 eq) under an atmosphere of nitrogen. The reaction was stirred at reflux temperature on an oil bath at 70°C for 2.5h. Internal temperature measured to be 45-50°C. TLC of the reaction run in ethyl acetate and developed with cerium ammonium molybdate and heating showed no change in the RF of the main spot.

The reaction was then cooled to room temperature, decanted from the unreacted zinc powder. The zinc powder was washed with ether and the combined solution of acetic acid and diethyl ether concentrated in high vacuum on a rotary evaporator. The gummy residue on evaporation was dissolved in ethyl acetate (50ml) and washed with water (50ml). The water layer was reextracted with ethyl acetate (2x25ml) and the combined organic extracts were separated, dried over sodium sulphate and concentrated in vacuum to give the desired product as a gum. 2.4g Crude product which was used directly in the next step

Before storage the gum was azeotroped with toluene (3x30ml) under high vacuum at room temperature to remove all traces of acetic acid and water.

A sample of The crude product was purified by flash column chromatography on silca gel (3 cm diameter column, 20 cm silica depth, eluting with 2:1 petrol: ethyl acetate to 1:1, the desired product having an Rf = 0.6 in neat ethyl acetate) giving a colourless oil (1.05 g, 55% for two steps). The oil was placed under high vacuum for 24 hours to remove trace solvents.

^{1}H NMR $CDCl_3$ (300 MHz) TMS ref. δ, 7.50-7.31 (5H, m, Ph), 5.58 (1H, s, $PhCHO_2$), 5.15 (1H, d, J= 2.9 Hz H^2), 4.80 (2H, AB, J = 7.4 Hz, OCH_2O), 4.61

(1H, s, H^1), 4.40-4.25 (1H, m, CHI, H^6), 4.17 (1H, dd, J = 2.9, 10.3 Hz, H^3), 3.95-3.85 (2H, m, H^4, H^6), 3.75-3.60 (2H, m, CH_2), 3.58 (3H, s, CH_3O), 3.51-3.42 (1H, m, H^5), 3.00-2.65 (2H, m, CH_2), 2.35 (2H, t, J = 7.4 Hz, CH_2), 1.90-1.30 (14H, m, CH_2), 1.15 (3H, t, J = 6.6 Hz, CH_3),

^{13}C NMR $CDCl_3$ (75 MHz) δ: 179.64 (CO), 137.31, 129.39, 128.48, 126.34 (Ph), 102.08 ($PhCHO_2$), 99.38 (C^1), 94.14 (OCH_2O), 83.57 (C^2), 77.46 (C^4), 71.31 (C^3), 68.59 (C^6), 67.78 (C^5), 64.11 (CH_2O), 57.58 (CH_3O), 34.22, 30.89, 30.67, 30.45, 29.57, 29.45, 29.36, 29.30, 24.95, 20.56 (CH_2), 15.09 (CH_3);

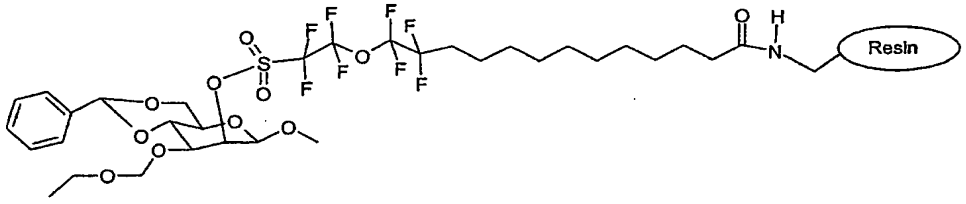
^{19}F NMR $CDCl_3$, (282 MHz) ref. C_6F_6 δ: 79.8, 74.2, 47.9, and 43.5.

m/z (ES^-) 803.3 $[M]^-$.

ν_{max} (film)/cm^{-1} 2929w, 2858w, 2858w, 1710m, 1411m, 1147s, 1093s, 1025s, 994s, 918s;

Example 1(iii)

Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13 ,15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside amino polystyrene resin amide



Crude Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13 ,15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-manno pyranoside from Example 1(ii) was dried by azeotroping with toluene (10ml) three times (804mg,1mmole) in dry dichloromethane (7.5ml) in a Corning 20ml centrifuge tube was treated with Aminopolystryene resin (Nova biochem 01-64-0143 1.4mmole/g, lot A24595, 500mg, 0.7mmole) , Diisopropylethylamine (260mg, 2mmole) and diphenylphosphoryl chloride (236mg, 1mmole). The reaction was shaken on a blood wheel at room temperature for 15h.

The resin was then collected by filtration and washed sequentially with

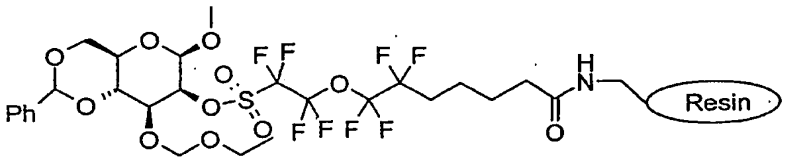
dichloromethane (100ml) and methanol (100ml) and ether (50ml). The resin was dried in high vacuum to constant weight to give 973mg of Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13 ,15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranosideAmino polystyrene Resin amide.

Gel phase NMR run by preparing a slurry of the resin in $CDCl_3$ and running as normal.

F^{19} NMR $CDCl_3$ $CFCl_3$ ref δ: 82.4, 88.5, 114.2, 118.58.

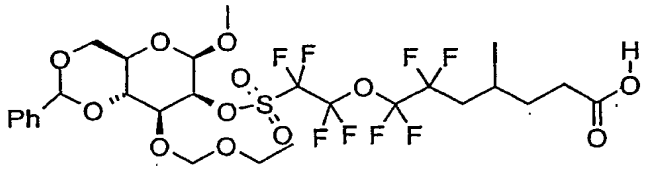
Example 2

Preparation of Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(8-oxa -6,6,7,7, 9,9,10,10-Octafluoro-decanioc acid-10-sulphonate)-β-D-mannopyranoside Amino polystyrene Resin amide



Example 2(i)

Preparation of Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(4-iodo 8-oxa -6,6,7,7, 9,9,10,10-Octafluoro-decanioc acid-10-sulphonate) -β-D-mannopyranoside



To Methyl-4,6-O-benzylidine-3-ethoxymethyl-2-(5-Iodooctafluoro-3-oxapentane sulphonate) -β-D-mannopyranoside (Intermediate 1) (400 mg, 0.54 mmol) and 4-pentenoic acid (56 mg, 0.56 mmol) in CH_3CN: H_2O (4 mL: 2 mL) was added $NaHCO_3$ (59 mg, 0.70 mol) and $Na_2S_2O_4$ (85%, 140 mg, 0.70

mmol) and the reaction stirred at room temperature for 20 mins. The reaction was concentrated *in vacuo*. Purification by silica gel column chromatography eluting with EtOAc: hexane (1: 2) afforded Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(4-iodo 8-oxa -6,6,7,7, 9,9,10,10-Octafluoro-decanioc acid-10-sulphonate) -β-D-mannopyranoside as a colourless oil 305 mg, 67 %).

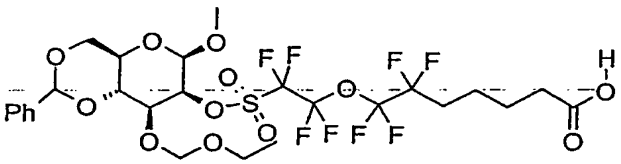
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.50-7.25 (5H, m, Ph), 5.52 (1H, s, $PhCHO_2$), 5.17 (1H, d, J = 2.9 Hz, H^2), 4.75 (2H, AB, J = 7.4 Hz, OCH_2O), 4.53 (1H, s, H^1), 4.34-4.24 (2H, m, H^6, CHI), 4.09 (1H, dd, J = 2.9 Hz, H^3), 3.90-3.77 (2H, m, H^4, H^6), 3.70-3.50 (2H, m, CH_2), 3.50 (3H, s, CH_3O), 3.45-3.32 (1H, m, H^5), 2.98-2.28 (4H, m, CH_2), 2.18-1.90 (2H, m, CH_2), 1.05 (3H, t, J = 7.4 Hz, CH_3);

^{13}C NMR (75 MHz, $CDCl_3$) δ: 177.32, 137.12, 129.28, 128.36, 126.20 (Ph); 101.93 ($PhCHO_2$), 99.19 (C^1), 94.02 (OCH_2O), 83.66 (C^2), 77.28 (C^4), 71.10 (C^3), 68.43 (C^6), 67.61 (C^5), 64.01 (CH_2O), 57.54 (CH_3O), 41.37, 35.14, 34.21, 19.09 (CH_2), 14.98 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ: 79.74, 72.97, 47.56, 43.89; *m/z* (ES^+) 740.9 $[M + Na]^+$, 1458.4 $[2M + Na]^+$.

ν_{max} (film)/cm^{-1} 2975w, 2878w, 1714m, 1410m, 1192s, 1146s, 1093s, 1025s, 994m, 920s;

Example 2(ii)

Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(4-iodo 8-oxa -6,6,7,7, 9,9,10,10-Octafluoro-decanioc acid-10-sulphonate) -β-D-mannopyranoside



To Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(4-iodo 8-oxa -6,6,7,7, 9,9,10,10-Octafluoro-decanioc acid-10-sulphonate) -β-D-mannopyranoside (prepared as described in Example 2(i)) (300 mg, 0.36 mmol) in Et_2O (2 mL) was added zinc (99.998%, 100 mesh, 93 mg, 1.42 mmol) and acetic acid (1 mL) and the reaction refluxed, under argon, for 3 h (bath temp = 80°C). The reaction was allowed to

cool to room temperature and filtered through celite, washing with Et_2O (50 mL). The filtrate was concentrated *in vacuo* to remove all of the solvent. Purification by silica gel column chromatography, eluting with EtOAc: hexane (1: 3), afforded Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(8-oxa -6,6,7,7, 9,9,10,10-Octafluoro-decanioc acid-10-sulphonate) -β-D-mannopyranoside as a colourless oil (70 mg, 27 %).

^1H NMR (300 MHz, $CDCl_3$) δ: 7.50-7.31 (5H, m, Ph), 5.58 (1H, s, $PhCHO_2$), 5.15 (1H, d, J = 2.9 Hz, H^2), 4.80 (2H, AB, J = 7.4 Hz, OCH_2O), 4.63 (1H, s, H^1), 4.36 (1H, q, J = 5.2 Hz, H^6), 4.17 (1H, dd, J = 2.9, 10.3 Hz, H^3), 3.95-3.86 (2H, m, H^4, H^6), 3.75-3.60 (2H, m, CH_2), 3.58 (3H, s, CH_3O), 3.52-3.43 (1H, m, H^5), 2.42 (2H, t, J = 7.4 Hz, CH_2), 2.20-2.00 (2H, m, CH_2), 1.80-1.60 (4H, m, CH_2), 1.15 (3H, t, J = 7.4 Hz, CH_3);

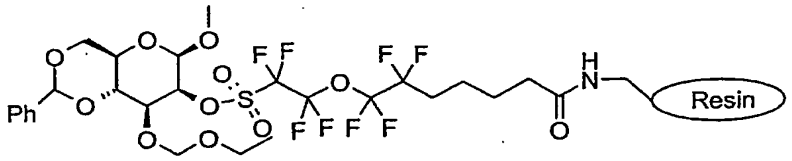
^{13}C NMR (75 MHz, $CDCl_3$) δ: 178.65 (CO), 137.11, 129.29, 128.37, 126.20 (Ph), 101.92 ($PhCHO_2$), 99.19 (C^1), 93.99 (OCH_2O), 83.50 (C^2), 77.27 (C^4), 71.08 (C^3), 68.42 (C^6), 67.60 (C^5), 64.00 (CH_2O), 57.54 (CH_3O), 33.55, 30.29, 24.16, 20.07 (CH_2), 14.97 (CH_3); ^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ: 79.72, 73.61, 47.91, 43.70;

m/z (ES^-) 719.0 $[M]^-$, 832.9 $[M + TFA]^-$.

ν_{max} (film)/cm^{-1} 2932w, 1723m, 1410m, 1192s, 1149s, 1115, 1027s, 922s;

Example 2(iii)

Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(8-oxa -6,6,7,7, 9,9,10,10-octafluoro-decanioc acid-10-sulphonate) -β-D-mannopyranoside amino polystyrene resin amide



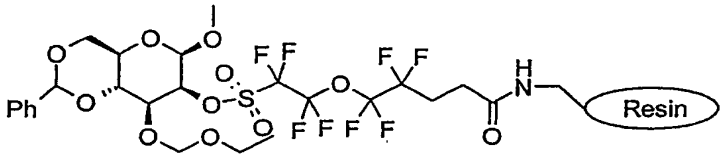
To amino-methylated polystyrene (NovaBiochem, 50-100 mesh, 01-64-0383, lot. A24063, loading: 1.5 mmol/g, 45 mg, 0.067 mmol) and Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(8-oxa -6,6,7,7, 9,9,10,10-octafluoro-decanioc acid-10-sulphonate) -β-D-mannopyranoside (prepared as described in Example 2(ii)) (58 mg, 0.081 mmol) in anhydrous CH_2Cl_2 (1 mL) was added *N,N-*

diisopropylethylamine (21 mg, 28 μL, 0.162 mmol), followed by diphenylphosphoryl chloride (19 mg, 16 μL, 0.081 mmol). The reaction was stirred gently, under argon, at room temperature for 18 h. The resin was removed by filtration, washed with CH_2Cl_2 (3 x 10 mL), CH_3OH (2 x 10 mL), Et_2O (5 x 5 mL) and dried *in vacuo*, at 40°C for 48 h. This gave methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(8-oxa -6,6,7,7, 9,9,10,10-octafluoro-decanioc acid-10-sulphonate) -β-D-mannopyranoside amino polystyrene resin amide as a pale yellow solid (87 mg, 99 %).

Loading: theoretical = 0.73mmol/g; found (F microanalysis) = 0.55mmol/g ν_{max} (on-bead)/cm^{-1} 2931w, 1662m, 1493m, 1452m, 1410m, 1275m, 1146s, 1094s, 1025s, 919s; ^{19}F NMR (282 MHz, $CDCl_3$, ref. $CFCl_3$) δ: ,-82.01, -88.13, -113.86, -118.23.

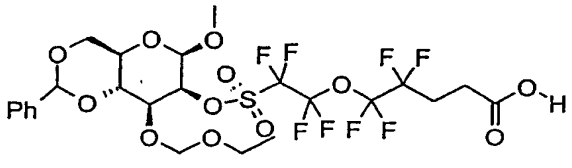
Example 3

Preparation of Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(6-oxa -4,4,5,5, 7,7,8,8-Octafluoro-decanioc acid-8-sulphonate) -β-D-mannopyranoside Amino polystyrene Resin amide



Example 3(i)

Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(6-oxa -4,4,5,5, 7,7,8,8-Octafluoro-decanioc acid-8-sulphonate) -β-D-mannopyranoside



To Methyl-4,6-O-benzylidine-3-ethoxymethyl-2-(5-Iodooctafluoro-3-oxapentane

sulphonate) -β-D-mannopyranoside (Intermediate 1), 1.0 g, 1.34 mmol) and acrylic acid (101 mg, 1.41 mmol) in CH_3CN: H_2O (8 mL: 4 mL) was added $NaHCO_3$ (135 mg, 1.61 mmol) and $Na_2S_2O_4$ (85%, 322 mg, 1.61 mmol) and the reaction stirred at room temperature for 45 mins. The reaction was concentrated *in vacuo*, dissolved in Et_2O (150 mL), washed with water (150 mL) and the aqueous phase re-extracted with Et_2O (100 mL). The combined organic phase was washed with brine (150 mL), dried (anhydrous $MgSO_4$) and concentrated *in vacuo*. Purification by silica gel column chromatography, eluting with EtOAc: hexane (1: 4) to EtOAc: hexane (1: 0), afforded the desired product as a colourless oil (419 mg, 38 %).

^1H NMR (300 MHz, $CDCl_3$) δ: 7.52-7.32 (5H, m, Ph), 5.58 (1H, s, $PhCHO_2$), 5.15 (1H, d, J = 2.9 Hz, H^2), 4.83 (2H, AB, J = 7.4 Hz, OCH_2O), 4.61 (1H, s, H^1), 4.30 (1H, q, J = 5.2 Hz, H^6), 4.16 (1H, dd, J = 2.9, 10.3 Hz, H^3), 3.90-3.78 (2H, m, H^4, H^6), 3.75-3.62 (2H, m, CH_2), 3.58 (3H, s, CH_3O), 3.51-3.42 (1H, m, H^5), 2.68 (2H, t, J = 7.4 Hz, CH_2), 2.55-2.36 (2H, m, CH_2), 1.65-1.15 (3H, t, J = 7.4 Hz, CH_3);

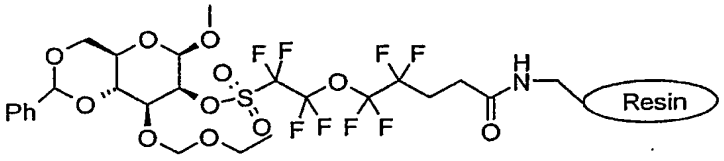
^{13}C NMR (75 MHz, $CDCl_3$) δ: 176.63 (CO), 137.11, 129.31, 128.38, 126.20 (Ph), 101.92 ($PhCHO_2$), 99.19 (C^1), 93.93 (OCH_2O), 83.61 (C^2), 77.23 (C^4), 71.09 (C^3), 68.41 (C^6), 67.58 (C^5), 64.01 (CH_2O), 57.54 (CH_3O), 25.97, 25.69 (CH_2), 14.94 (CH_3);

^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ: 79.82, 73.56, 47.73, 43.27; *m/z* (ES^-) 804.8 [M + TFA]$^-$, 1382.20 [2M]$^-$.

ν_{max} (film)/cm^{-1} 2972w, 1722m, 1412m, 1193s, 1148s, 1096s, 1026s, 921s;

Example 3(ii)

Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(6-oxa -4,4,5,5, 7,7,8,8-Octafluoro-decanioc acid-8-sulphonate) -β-D-mannopyranoside Amino polystyrene Resin amide



To amino-methylated polystyrene (NovaBiochem, 50-100 mesh, 01-64-0383, lot. A24063, loading: 1.5 mmol/g, 145 mg, 0.218 mmol) and the compound of

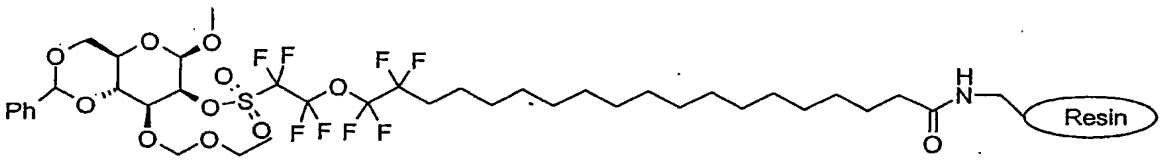
Example 3(i) (200 mg, 0.289 mmol) in anhydrous CH_2Cl_2 (2 mL) was added *N,N*-diisopropylethylamine (75 mg, 100 µL, 0.579 mmol), followed by diphenylphosphoryl chloride (68 mg, 55 µL, 0.289 mmol). The reaction was stirred gently, under argon, at room temperature for 18 h. The resin was removed by filtration, washed with CH_2Cl_2 (3 x 5 mL), CH_3OH (3 x 5 mL), Et_2O (5 x 5 mL) and dried *in vacuo*, at 40°C for 24 h. This gave the title resin as a pale yellow solid (283 mg, 94 %).

Loading: theoretical = 0.75mmol/g; found (F microanalysis) = 0.80mmol/g

^{19}F NMR (282 MHz, $CDCl_3$, ref. $CFCl_3$) δ: -81.84, -87.79, -113.67, -117.96.

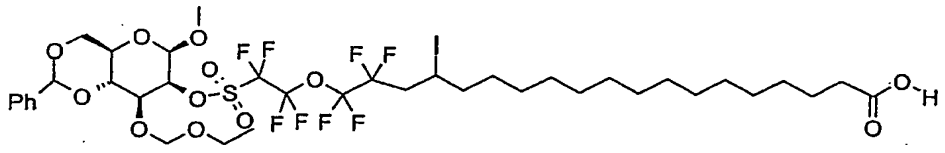
Example 4

Preparation of Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(20-oxa -18,18,19,19,21,21,22,22-Octafluoro-docosanoic acid-22-sulphonate) -β-D-mannopyranoside Amino polystyrene Resin amide



Example 4(i)

Methyl-4,6-O-benzylidene-3-ethoxymethyl-2-(16-iodo-20-oxa-18,18,19,19,21,21,22,22-Octafluoro-docosanoic acid-22-sulphonate) -β-D-mannopyranoside



The iodide (Intermediate 1, 1.0 g, 1.34 mmol) and 16-heptadecenoic acid (Apollo Scientific, 378 mg, 1.41 mmol) in CH_3CN (30 mL) formed a cloudy suspension. To this was added H_2O (20 mL) followed by $NaHCO_3$ (135 mg, 1.61 mmol) and

$Na_2S_2O_4$ (85%, 322 mg, 16.1 mmol) and the reaction stirred at room temperature for 10mins. A further portion of MeCN (25 mL) and H_2O (10 mL) was added but the reaction remained cloudy. After 1 h the reaction was concentrated *in vacuo*, dissolved in Et_2O (100 mL), washed with water (100 mL) and the aqueous phase extracted with Et_2O (50 mL). The combined organic phase was washed with brine (100 mL), dried (anhydrous $MgSO_4$) and concentrated *in vacuo* to give a crude white cloudy oil. Purification by silica gel column chromatography, eluting with EtOAc: hexane (1: 3), afforded Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(16-iodo-20-oxa -18,18,19,19,21,21,22,22-Octafluoro-docosanoic acid-22-sulphonate) -β-D-mannopyranoside as a colourless oil (230 mg, 17 %).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.50-7.31 (5H, m, Ph), 5.58 (1H, s, $PhCHO_2$), 5.15 (1H, d, J = 2.9 Hz, H^2), 4.85 (2H, AB, J = 7.4 Hz, OCH_2O), 4.63 (1H, s, H^1), 4.40-4.28 (1H, m, CHI, H^6), 4.17 (1H, dd, J = 2.9, 10.3 Hz, H^3), 3.97-3.87 (2H, m, H^4, H^6), 3.75-3.62 (2H, m, CH_2), 3.60 (3H, s, CH_3O), 3.52-3.42 (1H, m, H^5), 3.00-2.70 (2H, m, CH_2), 2.37 (2H, t, J = 7.4 Hz, CH_2), 1.85-1.40 (4H, m, CH_2), 1.30-1.10 (22H, m, CH_2), 1.15 (3H, t, J = 7.4 Hz, CH_3);

^{13}C NMR (100 MHz, $CDCl_3$) δ: 179.04 (CO), 137.56, 129.67, 128.76, 126.62 (Ph), 102.36 ($PhCHO_2$), 99.64 (C^1), 94.47 (OCH_2O), 84.00 (C^2), 77.59 (C^4), 71.55 (C^3), 68.87 (C^6), 68.06 (C^5), 64.41 (CH_2O), 57.91 (CH_3O), 42.02, 41.82, 41.62, 40.91, 34.48, 30.17, 30.14, 30.10, 29.99, 29.93, 29.81, 29.65, 29.10, 25.32 (CH_2), 21.79 (CHI), 15.40 (CH_3);

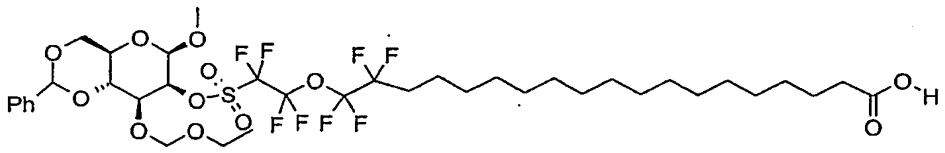
^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ: 80.20, 73.14, 47.87, 43.76;

m/z (ES^-) 1013.1 $[M]^-$, 1127.5 $[M + TFA]^-$.

ν_{max} (film)/cm^{-1} 2927w, 2855w, 1725m, 1412m, 1194s, 1149s, 1096s, 1026s, 921s;

Example 4(ii)

Preparation of Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(20-oxa -18,18,19,19,21,21,22,22-Octafluoro-docosanoic acid-22-sulphonate) -β-D-mannopyranoside



To Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(16-iodo-20-oxa -18,18,19,19,21,21,22,22-Octafluoro-docosanoic acid-22-sulphonate) -β-D-mannopyranoside (prepared as described in Example 4(i)) (200 mg, 0.204 mmol) in Et_2O (4 mL) was added zinc (99.998%, 100 mesh, 80 mg, 1.23 mmol) and acetic acid (2 mL) and the reaction refluxed, under argon, for 3 h (bath temp = 80°C). The reaction was allowed to cool to room temperature and decanted from the zinc, the zinc was washed with Et_2O (3 x 30 mL). The combined washings were concentrated *in vacuo*. Purification by silica gel column chromatography, eluting with EtOAc: hexane (1: 3), afforded Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(20-oxa -18,18,19,19,21,21,22,22-Octafluoro-docosanoic acid-22-sulphonate) -β-D-mannopyranoside as a colourless oil (132 mg, 75 %).

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.50-7.35 (5H, m, Ph), 5.60 (1H, s, $PhCHO_2$), 5.15 (1H, d, J = 2.9 Hz, H^2), 4.83 (2H, AB, J = 7.4 Hz, OCH_2O), 4.61 (1H, s, H^1), 4.36 (1H, q, J = 5.1 Hz, H^6), 4.20-4.12 (1H, m, H^3), 3.95-3.85 (2H, m, H^4, H^6), 3.75-3.60 (2H, m, CH_2), 3.58 (3H, s, CH_3O), 3.51-3.42 (1H, m, H^5), 2.37 (2H, t, J = 7.4 Hz, CH_2), 1.70-1.55 (4H, m, CH_2), 1.40-1.20 (26H, m, CH_2), 1.15 (3H, t, J = 7.4 Hz, CH_3);

^{13}C NMR (75 MHz, $CDCl_3$) δ: 179.40 (CO), 137.07, 129.51, 128.60, 126.45 (Ph), 102.19 ($PhCHO_2$), 99.49 (C^1), 94.28 (OCH_2O), 83.70 (C^2), 77.58 (C^4), 71.43 (C^3), 68.71 (C^6), 67.89 (C^5), 64.29 (CH_2O), 57.78 (CH_3O), 34.46, 31.02, 30.80, 30.58, 30.04, 29.99, 29.84, 29.80, 29.65, 29.49, 25.17, 21.43, 20.70 (CH_2), 15.21 (CH_3);

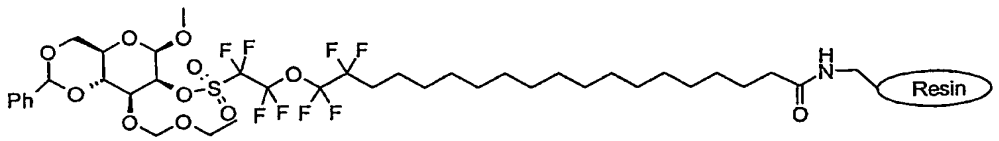
^{19}F NMR (282 MHz, $CDCl_3$, ref. C_6F_6) δ: 80.01, 74.08, 47.96, 43.34;

m/z (ES^-) 887.1 $[M]^-$.

ν_{max} (film)/cm^{-1} 2926w, 2854w, 1711m, 1412m, 1191, 1149s, 1096s, 1027s, 920s;

Example 4(iii)

Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(20-oxa -18,18,19,19,21,21,22,22-Octafluoro-docosanoic acid-22-sulphonate) -β-D-mannopyranoside Amino polystyrene Resin amide

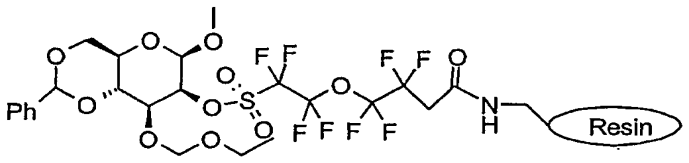


To amino-methylated polystyrene (NovaBiochem, 50-100 mesh, 01-64-0383, lot. A24063, loading: 1.5 mmol/g, 62 mg, 0.093 mmol) and Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(20-oxa -18,18,19,19,21,21,22,22-Octafluoro-docosanoic acid-22-sulphonate) -β-D-mannopyranoside (prepared as described in Example 4(ii)) (108 mg, 0.121 mmol) in anhydrous CH_2Cl_2 (3 mL) was added *N,N*-diisopropylethylamine (42μL, 0.243 mmol), followed by diphenylphosphoryl chloride (29 mg, 0.121 mmol). The reaction was stirred gently, under argon, at room temperature for 18 h. The resin was removed by filtration, washed with CH_2Cl_2 (3 x 10 mL), CH_3OH (3 x 10 mL), Et_2O (3 x 10 mL) and dried *in vacuo*, at 40°C for 48 h. This gave the Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(20-oxa -18,18,19,19,21,21,22,22-Octafluoro-docosanoic acid-22-sulphonate) -β-D-mannopyranoside Amino polystyrene Resin amide
as a pale yellow solid (136 mg, 86 %).

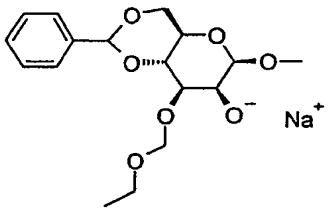
Loading: theoretical = 0.65mmol/g; found (F microanalysis) = 0.52mmol/g
^{19}F NMR (282 MHz, $CDCl_3$, ref. $CFCl_3$) δ: ,-82.06, -88.14, -113.93, -118.34.
ν_{max} (on-bead)/cm^{-1} 2925m, 1662m, 1493m, 1453m, 1411m, 1146m, 1095s, 1025s;

Comparitive Example 5

Preparation of Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(5-oxa -3,3,4,4,6,6,7,7-Octafluoro-decanioc acid-7-sulphonate) -β-D-mannopyranoside amino polystyrene resin amide

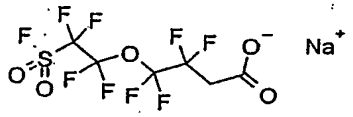


Example 5(i)



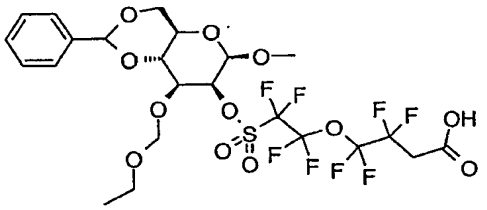
Methyl 4,6-O- benzylidene -3-ethoxymethyl -β-D-mannopyranoside (Intermediate 1(iv)) (0.5 g, 1.47 mmol) was dissolved in THF (10 mL) and NaH (1.1 eq., 1.62 mmol, 0.11 g) was added after washing with dry hexane. The mixture was heated at reflux for 15 minutes under nitrogen to give solution Methyl 4,6-O- benzylidene -3-ethoxymethyl -β-D-mannopyranoside sodium salt in THF.

Example 5(ii)



3,3,4,4,6,6,7,7, octafluoro-5-oxo-7-sulphonyl fluoride-heptanoic acid (1.5 eq., 0.79 g, 2.21 mmol) prepared as described in WO 02/055026 was dissolved in THF (10 mL) and NaH (1.1 eq,. 0.162 g, 2.43 mmol) was washed with dry hexane and added to give after stirring for fifteen minuites 3,3,4,4,6,6,7,7, octafluoro-5-oxo-7-sulphonyl fluoride-heptanoic acid sodium salt in THF.

Example 5(iii)



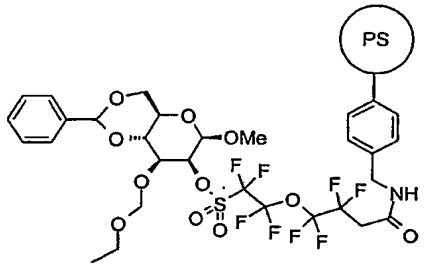
Methyl 4,6-O- benzylidene -3-ethoxymethyl -β-D-mannopyranoside sodium salt in THF (Example 5(i)) was added to 3,3,4,4,6,6,7,7, octafluoro-5-oxo-7-sulphonyl fluoride-heptanoic acid sodium salt in THF . (Example 5(ii)) by pipette and the mixture was stirred at RT for 24 hours under nitrogen. The frosty yellow solution was acidified with 99% acetic acid (6 eq.) and ethyl acetate (50 mL) and water (30 mL) added. The organic layer was separated and the aqueous layer extracted with ethyl acetate. The combined organic washings were dried over $MgSO_4$ and concentrated *in vacuo* to give a colourless yellow oil which was dried under high vacum for 3 hours. ^{19}F and ^{1}H NMR showed that the reaction gave 60% saturated EOM-mannose-linker in the crude product. This material was purified by reversed phase HPLC on a gilson automated reverse phase system. The fractions were partially evaporated on a rotary evaporator and freeze dried to give Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(5-oxa -3,3,4,4, 6,6,7,7-Octafluoro-decanioc acid-7-sulphonate) -β-D-mannopyranoside as a fluffy white solid (0.3 g, 30%).

^{1}H NMR $CDCl_3$ TMS ref δ: 7.44(2H, benzylidene phenyl), 7.35 (3H, benzylidene phenyl), 5.58 (s, 1H, benzylidene), 5.14 (d, 1H, H-2, J = 2.7 Hz), 4.80 (2H, 2 doublets, EOM-CH_2, J^2 = 7.5 Hz), 4.60 (s, 1H, H-1), 4.35 (dd, 1H, H-3, J = 5, 10.5 Hz), 4.12 (dd, 1H, H-4, J = 10.5, 10 Hz), 3.89 (2H, 2 quartets, ethyl CH_2), 3.70 (2H, two dt's, H-6), 3.56 (s, 3H, 1-OMe), 3.45 (1H, ddd, H-5), 3.08 (t, 2H, CH_2-CF_2), 1.09 (3H, t, methyl).

^{19}F NMR ($CDCl_3$, $CFCl_3$ reference): δ -82.5, -88.6, -114.3, -117.4.

$C_{23}H_{26}F_8O_{12}S$ requires C, 40.72%; H, 3.86%; F, 22.4%. Found: C, 40.53%; H, 3.94%; F, 21.52.

Example 5(iv)



Diisopropylethylamine (2 mmol, 0.26 g) was added to a solution of Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(5-oxa -3,3,4,4, 6,6,7,7-Octafluoro-decanioc acid-7-sulphonate) -β-D-mannopyranoside Example 5(iii) (0.442 mmol, 0.3 g), aminomethylated PS resin (0.398 mmol, 0.265 g) and diphenylphosphinic chloride (0.885 mmol, 0.21 g) in DCM (8 mL). The mixtures were agitated at RT for 3 hours. The supernatant was filtered off and the resin washed with a Diisopropylethylamine solution (3x2 mL) (20 mmol in DCM, 36 mL) and DCM then methanol 5 times. The resin was finally dried under vacuum to give Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(5-oxa -3,3,4,4, 6,6,7,7-Octafluoro-decanioc acid-7-sulphonate) -β-D-mannopyranoside amino polystyrene resin amide.

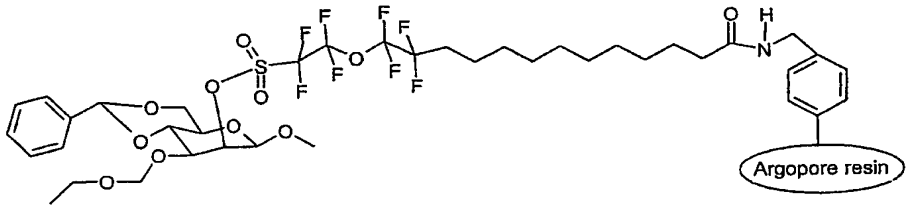
Gel phase ^{19}F NMR $CDCl_3$ ref $CFCl_3$: δ -82.4, -89.0, -114.3, -116.0

Elemental analysis/loading

Element	% Found	Calculated Loading mmol/g
N	1.25	0.89
F	6.89	0.45

Example 6

Preparation of Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(14-oxa -12,12,13,13, 15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside Amino methyl phenyl Argopore Resin amide



To Argopore (Argonaut Technologies, particle size = 134µm, 800047, lot. 00130, loading: 0.75 mmol/g, 200 mg, 0.15 mmol) and Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13 ,15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside Example 1 (ii) (157 mg, 0.195 mmol) in anhydrous CH_2Cl_2 (1.5 ml) was added *N,N* -diisopropylethylamine (50 mg, 67 µL, 0.39 mmol), followed by diphenylphosphoryl chloride (46 mg, 0.195 mmol). The reaction was stirred gently, under argon, at room temperature for 18 h. The resin was removed by filtration, washed with CH_2Cl_2 (3 x 5 ml), CH_3OH (3 x 5 ml), Et_2O (5 x 5 ml) and dried *in vacuo*, at 40°C for 24 h. This gave methyl -4, 6-O-benzylidene-3-ethoxymethyl-2-(14-oxa -12,12,13,13, 15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside Amino methyl phenyl Argopore Resin amide as a pale yellow solid (302 mg, 86 % (by weight)).

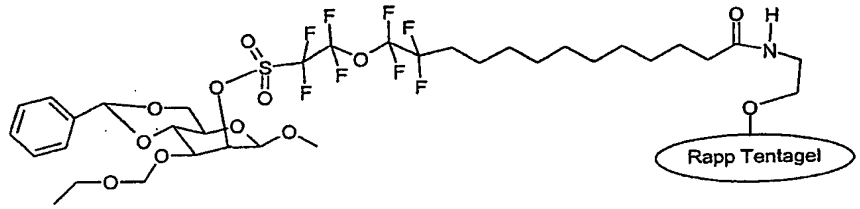
Loading: theoretical = 0.472mmol/g

ν_{max} (on-bead)/cm^{-1} 2928m, 1738s, 1493w, 1452m, 1414m, 1373m, 1216s, 1094s, 1026s, 919m;

^{19}F NMR (282 MHz, $CDCl_3$, ref. $CFCl_3$) δ: -82.07, -88.50, -113.65 (broad peaks)

Example 7

Preparation of Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(14-oxa -12,12,13,13, 15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside Amino ethoxy Tenta Gel Resin amide



To Tentagel S NH_2 (Rapp Polymere, particle size = 130µm, S30 132, loading: 0.25

mmol/g, 200 mg, 0.05 mmol) and Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13 ,15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside Example 1 (ii) (84 mg, 0.104 mmol) in anhydrous CH_2Cl_2 (2.5 mL) was added *N,N* -diisopropylethylamine (26.8 mg, 36 μL, 0.208 mmol), followed by diphenylphosphoryl chloride (24.6 mg, 0.104 mmol). The reaction was stirred gently, under argon, at room temperature for 18 h. The resin was removed by filtration, washed with CH_2Cl_2 (3 x 5 mL), CH_3OH (3 x 5 mL), Et_2O (5 x 5 mL) and dried *in vacuo*, at 40°C for 24 h. This gave Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(14-oxa -12,12,13,13, 15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside Amino ethoxy Tenta Gel Resin amide as a pale yellow solid (230 mg, 76 % (by weight)).

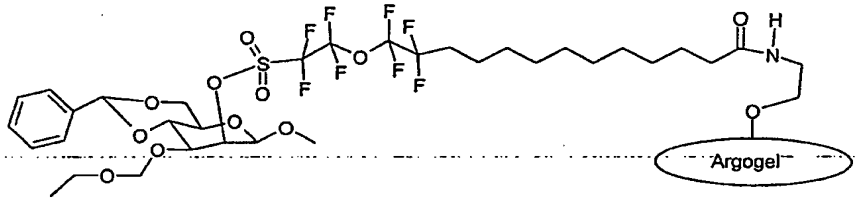
Loading: theoretical = 0.21mmol/g

ν_{max} (on-bead)/cm^{-1} 3459br, 2914m, 2875m, 1738m, 1453m, 1351m, 1216m, 1091s, 948m;

^{19}F NMR (282 MHz, $CDCl_3$, ref. $CFCl_3$) δ: -82.03, -88.10, -113.92, -118.22.

Example 8

Preparation of Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(14-oxa -12,12,13,13, 15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside Amino ethoxy Argogel Gel Resin amide



To Argogel (Argonaut Technologies, 800007, loading: 0.40 mmol/g, 200 mg, 0.08 mmol) and the Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13,15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-manno pyranoside Example 1 (ii) (55 mg, 0.065 mmol) in anhydrous CH_2Cl_2 (2.5 ml) was added *N,N* -diisopropylethylamine 17 mg, 23 μL, 0.13 mmol), followed by diphenylphosphoryl chloride (15.4 mg, 0.065 mmol). The reaction was stirred gently, under argon, at room temperature for 18 h. The resin was removed by

filtration, washed with CH_2Cl_2 (3 x 5 ml), CH_3OH (3 x 5 ml), Et_2O (5 x 5 ml) and dried *in vacuo*, at 40°C for 24 h. This gave Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(14-oxa -12,12,13,13, 15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside Amino alkyl LCAA-CPG Resin amide as a pale yellow solid (244 mg, 70 % (by weight)).

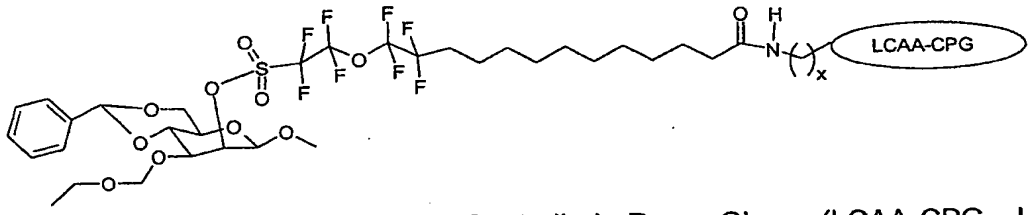
Loading: theoretical = 0.30 mmol/g

ν_{max} (on-bead)/cm^{-1} 3483br, 2914m, 2873m, 1738m, 1454m, 1350m, 1216m, 1092s, 948m;

^{19}F NMR (282 MHz, $CDCl_3$, ref. $CFCl_3$) δ: -82.01, -88.08, -113.91, -118.20.

Example 9

Preparation of Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(14-oxa -12,12,13,13, 15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside Amino alkyl LCAA-CPG Resin amide



To Long Chain Alkyl Amino Controlled Pore Glass (LCAA-CPG, Link Technologies, loading: 0.092 mmol/g, 200 mg, 0.0184 mmol) and Methyl-4,6-O-benzylidine-3-ethoxymethyl-2- (3-oxa -12,12,13,13 ,15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside Example 1 (ii)(30 mg, 0.037 mmol) in anhydrous CH_2Cl_2 (2 mL) was added *N,N*-diisopropylethylamine (9.5 mg, 13 μL, 0.074 mmol), followed by diphenylphosphoryl chloride (9 mg, 0.037 mmol). The reaction was rotated gently (not stirred to avoid shattering the glass beads), under argon, at room temperature for 18 h. The resin was removed by filtration, washed with CH_2Cl_2 (3 x 5 mL), CH_3OH (3 x 5 mL), Et_2O (5 x 5 mL) and dried *in vacuo*, at 40°C for 24 h. This gave Methyl-4, 6-O-benzylidene-3-ethoxymethyl-2-(14-oxa -12,12,13,13, 15,15,16,16-Octafluoro-hexadecanioc acid-16-sulphonate) -β-D-mannopyranoside Amino alkyl LCAA-CPG Resin amide as a

white solid (212 mg, 80 % (by weight)).
Loading: theoretical = 0.086mmol/g

Example 9: Radiolabelling

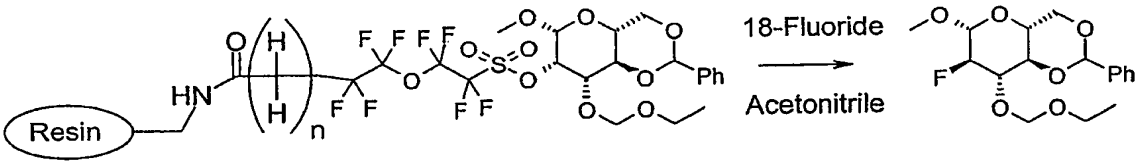
Procedure for the determination of the yield of FDG on treatment of a resin example with ^{18}F-Fluoride.

A carbon glass reaction vessel was placed in a brass heater and the pot lid (with three lines attached to allow evaporation, nitrogen flow, and addition of reagents) tightened down and the whole system was leak tested. Kryptofix (22mg) in acetonitrile (300ul) and potassium carbonate (8mg) in water (300ul), was transferred using a plastic syringe (1ml) into the carbon glass reaction vessel. The ^{18}F-fluoride was added and heated to 125°C. At 15mins three aliquots of acetonitrile (0.5ml) were added at 1 minute intervals. ^{18}F-Fluoride was dried up to 40mins in total. The heater was cooled to room temperature, the pot lid removed and acetonitrile (0.2ml) was added. The pot lid was replaced and the lines were capped off with stoppers. The heater was set at 100°C for 10 minutes and the ^{18}F-fluoride redissolved. After cooling to room temperature once more using a plastic syringe (1ml), the acetonitrile (0.2ml) was transferred to a second carbon glass reaction vessel containing the resin (20-25mg). This carbon glass vessel was transferred to an ion chamber and the labelling activity measured. The carbon glass vessel was replaced in the brass heater and the capped pot lid was tightened down. The reaction was heated to 86°C for 4mins before cooling with compressed air. The pot lid was removed acetonitrile (1ml) was added and the activity in the reaction vessel was measured. Using a plastic syringe (5ml) and beige needle (19Gx2"), the resin was mixed and drawn up in to the plastic syringe (5ml). The reaction mix was then syringed through a sintered syringe and into a collection vial. The reaction vessel was washed with a further volume of acetonitrile (0.5ml) and passed through the sintered syringe. The activity in the collection vial and also on the resin and sintered syringe was measured.

Samples were taken for RP HPLC analysis to determine the incorporation yield of ^{18}F-fluoride into the protected sugar.

Results

Radiochemical yield of protected FDG as a function of the number of CH_2's in the linker



The yield of protected FDG on treatment of Examples (1-5) with fluoride ion is shown in Table 1.

Table 1

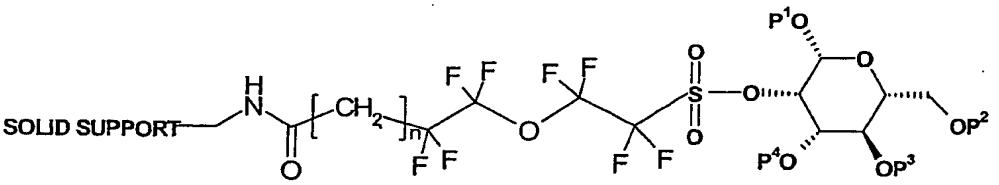
Example number	n (CH_2's In linker)	Radiochemical yield %	Fluoride remaining Unreacted %
5	1	45-50	50-55
3	2	75.0	25
2	4	92.3	7.7
1	10	85-90	10-15
4	16	77	23

Example 10 : Deprotection Procedure

The solution eluted from the resin was then passed through a silica SepPak cartridge to remove fluoride. The solution collected was placed into a clean carbon glass reaction vessel and the activity was measured in the ion chamber. The carbon glass vessel was then heated to 100°C for 10mins to evaporate the solvent, before cooling. HCl (6M,0.5ml) was added and heated in a closed system at 120°C for 5 minutes. After neutralisation with NaOH the reaction mixture was analysed using ion chromatography.

Claims

1. A compound of formula (I):



(I)

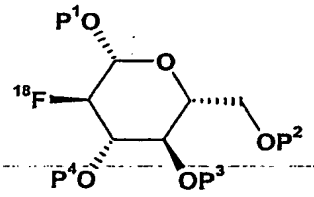
wherein P^1, P^2, P^3, and P^4 are each independently hydrogen or a protecting group; and n is an integer of from 2 to 20.

2. A compound of formula (I) according to claim 1 in which n is 4 to 12.

3. A compound of formula (I) according to claim 1 or 2 in which n is 6 to 10.

4. A compound of formula (I) according to any of claims 1 to 3 in which n is 10.

5. A process for the production of 2-^{18}F-fluoro-2-deoxy-D-glucose (^{18}F-FDG) which comprises treatment of a compound of formula (I) according to any of claims 1 to 4,
with $^{18}F^-$ to produce the labelled tracer of formula (II)



(II)

wherein P^1, P^2, P^3, and P^4 are each independently hydrogen or a protecting group; optionally followed by
(i) removal of excess $^{18}F^-$, for example by ion-exchange chromatography; and/or
(ii) removal of the protecting groups; and/or
(iii) removal of organic solvent; and/or

(iv) formulation of the resultant compound of formula (II) as an aqueous solution.

6. A radiopharmaceutical kit for the preparation of ^{18}F-FDG for use in PET, which comprises:

(v) a vessel containing a compound of formula (I) according to any of claims 1 to 4 ; and

(vi) means for eluting the vessel with a source of $^{18}F^-$;

(vii) an ion-exchange cartridge for removal of excess $^{18}F^-$; and optionally

(viii) a cartridge for solid-phase deprotection of the resultant product of formula (II) as defined in claim 5 .

7. A cartridge for a radiopharmaceutical kit for the preparation of an ^{18}F-FDG for use in PET which comprises:

(i) a vessel containing a compound of formula (I) according to any of claims 1 to 4; and

(ii) means for eluting the vessel with a source of $^{18}F^-$.

8. A method for obtaining a diagnostic PET image which comprises the step of using a radiopharmaceutical kit or a cartridge for a radiopharmaceutical kit according to claim 6 or 7.